PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2008/010487	05.09.2008	07.09.2007

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/00 A61M5/14 A61F2/02 A61F9/00

Applicant
QLT PLUG DELIVERY, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Glikman, J Telephone No. +31 70 340-3055

Form PCT/ISA/237 (Cover Sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2008/010487

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	at most 15-19, 22-27, 31-32,35-40,42-47,49-77,89-92,100-102.
	No:	Claims	at least 1-14,20-21,28-30,33-34,41,48,78-88,93-99,103.
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-299
Industrial applicability (IA)	Yes:	Claims	1-299
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 03/022242 A (SMART DRUG SYSTEMS INC.) 20 March 2003
D2: WO 02/058667 A (BAUSCH & LOMB INC.) 1 August 2002
D3: US 2006/020248 A1 (A. PRESCOTT) 26 January 2006
D4: US-A-5 283 063 (J. FREEMAN) 1 February 1994
D5: WO 2006/057859 A (THERAKINE CORP.) 1 June 2006
D6: WO 2007/115259 A (FORSIGHT LABS, LLC) 11 October 2007
D7: WO 2008/094989 A (ALCON RESEARCH, LTD) 7 August 2008
D8: US 2007/243230 A1 (E. DE JUAN ET AL.) 18 October 2007 cited in the application

1. Present claims 1-299 are allowable.

2. Claims 273-278 relate to a therapy. The patentability of claims 273-278 is *inter alia* dependent upon their formulation as well as upon national and regional laws and no unifying criteria is provided in this field by the PCT. Their assessment will be carried out based on the alleged effects of the devices searched in the International Search Report.

3. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-14, 20-21, 28-30, 33-34, 41, 48, 78-88, 93-99, 103, 106-108, 110-114, 122-123, 125, 131-133, 138-146, 151-156, 158-159, 166, 169-183, 185, 187, 190-191, 193-196, 199, 207, 209, 216-217, 219, 226, 233-235, 271-272, 279, 297-298 is not new in the sense of Article 33(2) PCT.

3.1 The document D1 discloses partially covered rods (see D1, page 4, lines 2-6) containing recombinant growth hormones (see examples 1-3 of D1) or ivermectin, an

anthelmintic (see example 4) in a silicone matrix. The silicone matrix is crosslinked with a platinum compound. The sheath according to present claim 1 is also a silicone in D1. The rods of D1 make subcutaneous implants in calves (see D1, example 5)
D1 is prejudicial to the novelty of the subject-matter of claims 1-7, 9-13, 20-21, 28-30, 33-34, 41, 48, 78-88, 93-99, 103, 106-108, 110-114, 122-123, 125, 131-133, 138-146, 151-156, 158-159, 166, 169-183, 185, 187, 190-191, 193-196, 199, 207, 209, 216-217, 219, 226, 233-235, 271-272, 279, 297-298 insofar as said claims may be understood (see item VIII, point 5 under).

3.2 Document D4 discloses a HEMA hydrogel coated with a hydrophobic PTFE coating for use as a punctum plug (see D4, col.13-14, claim 1). The therapeutic agent according to present claim 1 is water and the polymer according to present claim 1 is HEMA.
Document D4 is prejudicial to the novelty of the subject-matter of at least claims 1, 8 and 14 insofar as said claims may be understood (see item VIII, point 5 under).

4. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-299 does not involve an inventive step in the sense of Article 33(3) PCT.

4.1 The subject-matter of claims 1-14, 20-21, 28-30, 33-34, 41, 48, 78-88, 93-99, 103, 106-108, 110-114, 122-123, 125, 131-133, 138-146, 151-156, 158-159, 166, 169-183, 185, 187, 190-191, 193-196, 199, 207, 209, 216-217, 219, 226, 233-235, 271-272, 279, 297-298, insofar as said claims may be understood (see item VIII, point 5 under), does not rely on an inventive step in view of D1 and D4 since said subject-matter is known (see point 3 above).

4.2 The other independent claims are mere variations of the known subject-matter of D1 and D4, which subject-matter stands within reach of the skilled man performing his daily routine.
The other dependent claims of the present set of claims do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see documents D1-D5 and the corresponding

passages cited in the search report. In particular, a polyimide sheath according to present examples is known in the art (see D5, claim 2).

Re Item VI

D6-D7 are patent applications with priority dates preceding the priority dates of present application, but published after the filing date of present application. These documents D6-D7 are not taken into account in the PCT-chapter II procedure but may be relevant for assessing novelty of the present subject-matter in the regional phase of the PCT examination procedure.

Re Item VIII

1. Although claims 1, 80, 108, 140, 272, 280, 285 and 298 have been drafted as separate independent claims of devices, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

2. Although claims 170 and 171 have been drafted as separate independent claims of manufacturing methods, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

3. Present examples in the description from page 166, line 4 to page 182, line 2 relate to ophthalmological implantable devices made of a core containing a cured polydimethylsiloxane elastomer with an ophthalmological drug. Said core is located in a polyimide tube. Said devices display a controlled release of the drug.

4. In view of the limitation of the subject-matter of the examples (see point 3 above), present claims 1-299 as a whole lack conciseness.

5. Present claim 1 contravenes Art. 6 PCT for the reasons below:
-it is an undue generalisation of the subject-matter really disclosed in the description (see point 3 above).
- it lacks essential features which may provide the claimed devices a controlled release when implanted in a biological medium, creating an undue burden to the skilled man when performing the claimed invention.
- it lacks support in the description in all the embodiments not covered by the present examples (see point 3 above). In particular core-shell particles, coated granules, polyurethane matrixes, dual release of active agents, sheaths containing multiple inserts and macroporous sheaths are not supported by the description.
- With the wording " adapted for disposition within an implant" the claim attempts to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

5. Objection of point 5 above also partially applies to present claims 2-299.

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Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)

General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT). If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003